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Summary of Investigation Results

Regorafenib hydrate

July 17, 2024

Non-proprietary name

Regorafenib hydrate

Brand name (marketing authorization holder)

Stivarga tablets 40mg (Bayer Yakuhin, Ltd.)

Japanese market launch

May 2013

Indications

•Unresectable, advanced or recurrent colorectal cancer

•Gastrointestinal stromal tumour that has progressed after cancer chemotherapy

•Unresectable hepatocellular carcinoma that has progressed after cancer chemotherapy

Summary of revisions

1. The language concerning neutropenia and leukopenia should be added to the 8. IMPORTANT PRECAUTIONS section.
2. “Neutropenia” and “leukopenia” should be added to the 11.1 Clinically Significant Adverse Reactions section in 11. ADVERSE REACTIONS.

Investigation results and background of the revision

Cases involving neutropenia and/or leukopenia were evaluated. Cases for which a causal relationship of regorafenib hydrate to neutropenia and/or leukopenia was reasonably possible have been reported. As a result of consultation with expert advisors regarding the causality assessment of the cases and the necessity of revision of PRECAUTIONS, the MHLW/PMDA concluded that revision of PRECAUTIONS was necessary.

Pharmaceuticals and Medical Devices Agency

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Reference: Number of cases*† and patient mortalities of neutropenia and/or leukopenia reported in Japan

Cases involving neutropenia

A total of 18 cases have been reported to date. (A causal relationship between the drug and event was reasonably possible for 14 cases, including 2 cases in which the drug was administered outside the approved indication or was administered inappropriately.)

No patient mortalities have been reported to date.

Cases involving leukopenia

A total of 13 cases have been reported to date. (A causal relationship between the drug and event was reasonably possible for 11 cases, including 2 cases in which the drug was administered outside the approved indication or was administered inappropriately.)

No patient mortalities have been reported to date.

*: Cases collected in the PMDA's database for adverse drug reactions, etc. reports

†: Cases of grade 3 or higher by the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0

The expert advisors present at the Expert Discussion regarding the current investigation were nominated based on their conflict of interest declarations concerning the relevant products, pursuant to the “Rules for Convening Expert Discussions, etc., by the Pharmaceuticals and Medical Devices Agency” (PMDA Administrative Rule No. 20-8, dated December 25, 2008).

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